3. Schattner A, Gilad A, Cohen J. Systemic granulomatosis and hypercalcaemia following intravesical bacillus Calmette-Guérin immunotherapy. *J Intern Med.* 2002;251:272–277.
4. Buchs N, Chevrel G, Miossec P. Bacillus Calmette-Guérin induced aseptic arthritis: an experimental model of reactive arthritis. *J Rheumatol.* 1998;25:1662–1665.
5. Mas AJ, Romera M, Valverde Garcia J. Articular manifestations after the administration of intravesical BCG. *Joint Bone Spine.* 2002;69:92–98.
6. Shoenfeld Y, Aron-Maor A, Tanai A, Ehrenfeld M. BCG and autoimmunity: another two-edged sword. *J Autoimmun.* 2001;16:235–240.
7. Smith MD, Chandran G, Parker A, et al. Synovial membrane cytokine profiles in reactive arthritis secondary to intravesical bacillus Calmette-Guérin therapy. *J Rheumatol.* 1997;24:752–758.
8. Bartolomé Pacheco MJ, Martinez Taboada VM, Blanco R, Rodriguez Valverde V, Valle JI, López Hoyos M. Reactive arthritis after BCG immunotherapy: T cell analysis in peripheral blood and synovial fluid. *Rheumatology.* 2002;41:1119–1125.
9. Baxter AG, Horsfall AC, Healey D, et al. Mycobacteria precipitate an SLE-like syndrome in diabetes-prone NOD mice. *Immunology.* 1994;83:227–231.
10. Engelman EG, Sonnenfield G, Dauphinee M. Treatment of NZB/NZW f1 hybrid mice with *Mycobacterium bovis* strain of BCG or type II interferon preparations accelerates autoimmune disease. *Arthritis Rheum.* 1981;323:1381–1387.

CLINICAL AND BIOLOGICAL DISTINCTIONS BETWEEN TYPE I AND TYPE II ACQUIRED ANGIOEDEMA

To the Editor:

Acquired angioedema related to C1Inh deficiency is characterized by nonpruritic subcutaneous or mucous swellings, adult onset of symptoms (after the fourth decade), and lack of evidence of inheritance of the disorder. It is classified into two types: type I, which is mostly associated with B-cell proliferative disorders following accelerated catabolism of normally biosynthesized C1Inh, and type II, which is defined by the presence of an autoantibody against the C1Inh protein (1,2). We report the clinical and biological characteristics of 18 unrelated patients with acquired angioedema who were studied from 2000 to 2002.

Table 1. Clinical and Biological Characteristics of Patients with Type I or Type II Acquired Angioedema

Characteristic	Type I Acquired Angioedema (n = 9)	Type II Acquired Angioedema (n = 9)	*P* Value
	Number (%) or Mean ± SD		
Male sex	3 (33)	6 (67)	
Age of onset (years)	61 ± 10	63 ± 10	
Localization of edema			
Limbs	2 (22)	5 (56)	
Face	9 (100)	5 (56)	<0.05
Abdomen	2 (22)	3 (33)	
Larynx	6 (67)	5 (56)	
Frequency of attack (per year)	4 ± 4	8 ± 4	
Severe events	0	1 death; 1 tracheotomy	
Hypertension	1 (11)	5 (56)	<0.05
Associated diseases	7 (78)*	6 (67)†	
ACE inhibitor use at time of diagnosis	0	4 (44)	<0.05
Treatment			
Danazol	2 (22)	8 (89)	
Tranexamic acid	0	2 (22)	
Corticosteroids	3 (33)	2 (22)	
Immunosuppressive drugs	2 (22)	1 (11)	
Biological assays‡			
Antigenic C1Inh (reference, 210–345 mg/L)	76 ± 48	156 ± 80	0.03
Frequency of normal values	0%	33%	0.06
C1Inh activity (reference, 17.2–27.4 U/mL)	4.8 ± 2.6	3.6 ± 2.3	
Frequency of normal values	0%	0%	
Antigenic C4 (reference, 157–257 mg/L)	44.2 ± 38.4	56.6 ± 54.6	
Frequency of normal values	0%	11%	
Antigenic C1q (reference, 88%–116% pool of normal human serum)	44 ± 48	64 ± 46	
Frequency of normal values	22%	38%	
Anti-C1Inh antibody (% of titers >10 U)	0%	IgG: 56% IgM: 33% IgA: 11%	

* Included lymphoma (n = 2 patients), myeloma (n = 1), monoclonal component (n = 1), and autoimmune disease (n = 3).
† Included monoclonal component (n = 6 patients).
‡ Antigenic levels of C1Inh, C4, and C1q were measured using nephelometric assays; C1Inh activity was measured using the method of Drouet et al (3); and anti-C1Inh antibody levels were measured using enzyme-linked immunosorbent assays.
ACE = angiotensin-converting enzyme; Ig = immunoglobulin.

Nine patients with anti-C1Inh antibody titers >10 U were considered as having type II acquired angioedema; the remaining patients with titers <8 U were considered as having type I disease. Type I patients were more likely to have facial edema, but fewer attacks in general, as compared with type II patients (Table). Severe events

were observed in 2 type II patients, but in none of the type I patients. Type II patients had monoclonal component (with the same isotype as anti-C1Inh antibody) when angioedema was diagnosed. Most type I patients had lymphoproliferative disorders or systemic diseases when angioedema was diagnosed. Five type II patients presented with hypertension, as compared with 1 patient with type I disease. Four type II patients were treated with angiotensin-converting enzyme (ACE) inhibitors when they had the first angioedema attack, as compared with none with type I disease. These drugs are known to trigger attacks of angioedema by inhibition of bradykinin degradation (4). Discontinuation of ACE inhibitor use did not affect the course of angioedema.

Patients also differed in biological assay results (Table). All type I patients had low antigenic C1Inh levels, whereas 3 type II patients had normal levels. Treatment procedures also varied among patients (Table). Danazol was prescribed most frequently; it was effective, but patients often needed high daily doses (100 to 600 mg/d). Tranexamic acid, which was rarely used, was effective in only 1 patient with type II disease. A good clinical response was observed in all 3 patients with type I disease who were taking corticosteroids, as well as in 1 of the 2 patients with type II disease. Immunosuppressive drugs were clinically effective in type I patients, with partial restoration of biological activity. However, the 1 patient with type II disease who took immunosuppressive drugs died (laryngeal edema). In conclusion, the data suggest that danazol would be effective in the treatment of acquired angioedema, although tranexamic acid, which was rarely used in these patients, may also be a good rational prophylactic choice as proposed by Cugno et al (5).

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1. Markovic S, Inwards D, Frigas E, Phyliky R. Acquired C1 esterase inhibitor deficiency. *Ann Intern Med.* 2000;132:144–150.
2. Cicardi M, Bisiani G, Cugno M, Späth P, Agostoni A. Autoimmune C1 inhibitor deficiency: report of eight patients. *Am J Med.* 1993;95:169–175.
3. Drouet C, Alibeu C, Ponard D, Arlaud GJ, Colomb MG. A sensitive method to assay blood complement C1 inhibitor activity. *Clin Chim Acta.* 1988;174:121–130.
4. Nussberger J, Cugno M, Cicardi M. Bradykinin mediated angioedema. *N Engl J Med.* 2002;347:621–622.
5. Cugno M, Cicardi M, Agostini A. Activation of the contact system and fibrinolysis in autoimmune acquired angioedema: a rationale for prophylactic use of tranexamic acid. *J Allergy Clin Immunol.* 1994;93:870–876.

RHABDOMYOLYSIS ASSOCIATED WITH PROBABLE SARS

To the Editor:

Severe acute respiratory syndrome (SARS) is an emerging disease that was first recognized in November 2002 (1). Previous studies have pointed out that patients with probable SARS may have abnormal laboratory examination results, including elevated creatine kinase levels (2–4). We report 3 patients with probable SARS who developed rhabdomyolysis.

The first patient was a 38-year-old woman who suffered from probable SARS during a nosocomial outbreak in Taiwan (5). She developed fever and chills on April 20, 2003. Her chest radiograph showed bilateral pneumonic patches. Because SARS was suspected, she was admitted to our hospital on April 28. She was intubated and given midazolam and succinylcholine for respiratory failure. Fever of up to 39°C was noted on the same day. Repeat blood, urine, and sputum cultures did not yield any pathogens. Vero cells from a throat swab yielded a coronavirus. SARS-associated coronavirus infection was confirmed by detection of coronavirus ribonucleic acid by real-time reverse transcription polymerase chain reaction tests from sputum. Serum creatine kinase level increased from 21 to 13,834 U/L from May 2 to 3, while serum creatinine level increased to 3.27 mg/dL. By May 6, serum creatine kinase level had increased to a peak value of 339,750 U/L, even after hydration and alkalization, while serum myoglobin level had increased to 167 ng/mL (normal, $<$70 ng/mL). Rhabdomyolysis was diagnosed clinically. Acute renal failure developed on May 4 and the patient went into a deep coma. She died 3 weeks later due to secondary bacterial infection despite mechanical ventilatory support, hemodialysis, and antibiotic treatment. A skeletal muscle biopsy specimen showed necrotic muscle fibers, basophilic change of sarcoplasm, enlarged vesicular nuclei, and centrally located nuclei.

The second patient was a 52-year-old-man who suffered from probable SARS during a nosocomial outbreak at the same hospital (5). He started to have fever and chills since April 21, with myalgia and headache. A dry cough developed since April 24 and a chest radiograph revealed a pneumonia patch over the right lower lung field. Acute respiratory distress syndrome and hypotension developed on April 26. Initial microbiologic workup that included blood, urine, and sputum cultures was negative, except for Vero cells from a throat swab, sputum, and stool that were positive for coronavirus. Indirect fluorescent antibody to SARS-associated coronavirus was also positive.